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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/620,091

07/15/2003

Steve Roffler

4910-2DIV2

8710

7590

11/20/2006

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EXAMINER

FETTEROLF, BRANDON J

ART UNIT

PAPER NUMBER

1642

DATE MAILED: 11/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/620,091

Applicant(s)

ROFFLER ET AL.

Examiner

Brandon J. Fetterolf, PhD

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 August 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 21-25, 27-33 and 35-39 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 21-25, 27-33 and 35-39 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/29/2006 has been entered.

Claims 21-25, 27-33 and 35-39 are currently pending and under consideration.

Specification

The specification **remains** objected to as failing to provide proper antecedent basis for the claimed subject matter in claims 38 and 39. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o).

Correction of the following is required:

For each deposit made pursuant to the regulations for Deposit of Biological Material set forth in MPEP 1801, the specification shall contain:

- (1) The accession number for the deposit;
- (2) The date of the deposit;
- (3) A description of the deposited biological material sufficient to specifically identify it and to permit examination; and
- (4) The name and address of the depository.

Claim Objections

Claim 25 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In the instant case, claim 25 does not appear to further limit

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independent claim 21. If Applicants were to amend claim 25 to recite "said polyethylene glycol-containing compound comprises β -glucuronidase", the objection would be withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-25, 27-33 and 35-39 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the claims are inclusive of a genus of polyethylene glycol-containing compounds, which are cleared by an anti-polyethylene glycol antibody, and a genus of polyethylene glycol-containing conjugates comprising a tumor targeting means and a means for activating a genus of anti-tumor prodrug used for treating a tumor. However, the written description in this case only sets forth a polyethylene glycol-containing compound consisting of a PEG-modified β G which may be further covalently linked to a F(ab)₂ fragment of mAb B72.3 or mAb H25 and one species of polyethylene glycol-conjugates used for the treatment of a tumor, wherein the tumor targeting "agent" is a F(ab)₂ fragment of mAb B72.3 covalently linked to a PEG-modified β G which activates one species of prodrug referred to as the tetra n-butyl ammonium salt of glucuranoid derivative of p-hydroxyaniline mustard.

The specification teaches (page 8, lines 11-13) that specific polyethylene glycol-containing compounds of the invention include, but are not limited to, compounds which are cleared from the circulation by an antibody against PEG with out significant toxic side effects. The specification further teaches (page 8, lines 9-11 and page 9, lines 7-9) the development of PEG-modified compounds which are useful in cancer therapy, wherein the PEG-containing compound comprises a tumor targeting means and a means for activating an anti-tumor prodrug to the patient. Although the specification (page 19) discloses the accelerated clearance of two polyethylene glycol containing

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compounds comprising a PEG-modified β G covalently linked to mAb's B72.3 or H25, the written description (page 43, lines 3+) only reasonably conveys one species polyethylene glycol-conjugates used for the treatment of a tumor, wherein the tumor targeting "agent" is a $F(ab)_2$ fragment of mAb B72.3 covalently linked to a PEG-modified β G which activates one species of prodrug referred to as the tetra n-butyl ammonium salt of a glucuronoid derivative of p-hydroxyaniline mustard. A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common the genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cNDA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus."

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., ___ F.3d ___, 2004 WL 260813, at *9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genus. That is, the specification provides neither a representative number of compounds that encompass the genus of polyethylene glycol-containing compound which are rapidly cleared from blood circulation by administration of an anti-polyethylene glycol antibody nor does it provide a description of structural features that are common to the compounds. Further, the specification fails to provide a representative number of conjugates that encompass the genus of polyethylene glycol-containing conjugates comprising a tumor targeting means and a means for activating a genus of anti-tumor prodrug used for treating a tumor nor does it provide a description of structural features that are common to the conjugates. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of two species of polyethylene glycol-containing compounds, which are cleared by an anti-polyethylene glycol antibody and one species of polyethylene glycol-containing conjugates comprising one tumor targeting means and one means for activating a single anti-tumor prodrug used for treating a tumor is insufficient to describe the genus. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

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Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure(s) of the encompassed genus of polyethylene-glycol containing compounds and conjugates, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF’s were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only two species of polyethylene glycol-containing compound consisting of a PEG-modified β G which may be further covalently linked to a F(ab)₂ fragment of mAb B72.3 or mAb H25 and one species of polyethylene glycol-conjugates used for the treatment of a tumor, wherein the tumor targeting “agent” is a F(ab)₂ fragment of mAb B72.3 covalently linked to a PEG-modified β G which activates one species of prodrug referred to as the tetra n-butyl ammonium salt of glucuranoid derivative of p-hydroxyaniline mustard, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

In response to this rejection, Applicants contend that claims 21-29 have been amended to recite that the compounds are limited to those capable of binding to an anti-polyethylene glycol monoclonal antibody that is produced by immunizing a mouse with a RH1- β G-PEG conjugate, and that the anti-polyethylene glycol monoclonal antibody is limited to that which is produced by immunizing a mouse with a RH1- β G-PEG conjugate.

These arguments have been carefully considered, but are not found persuasive.

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In response to these arguments, the Examiner acknowledges that independent claims 21 and 29 have been amended to recited that the polyethylene glycol-containing compound is capable of binding to an anti-polyethylene glycol monoclonal antibody that is produced by immunizing a mouse with a RH1-bG-PEG conjugate". However, the Examiner recognizes the Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical characteristics and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (Federal register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3) and (see MPEP 2164). In the instant case, the amendment appears to characterize the anti-PEG monoclonal antibody, and does not appear to "characterize" the PEG-containing compound. Therefore, only two species of polyethylene glycol-containing compound consisting of a PEG-modified β G which may be further covalently linked to a $F(ab')_2$ fragment of mAb B72.3 or mAb H25 and one species of polyethylene glycol-conjugates used for the treatment of a tumor, wherein the tumor targeting "agent" is a $F(ab')_2$ fragment of mAb B72.3 covalently linked to a PEG-modified β G which activates one species of prodrug referred to as the tetra n-butyl ammonium salt of glucuranoid derivative of p-hydroxyaniline mustard, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph.

Therefore, No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

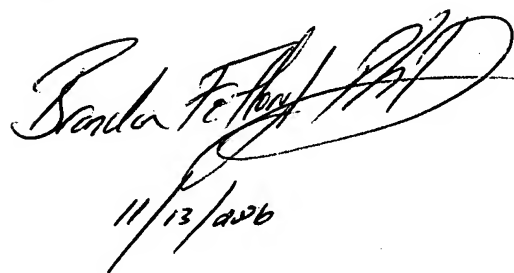
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brandon J Fetterolf, PhD
Patent Examiner
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BF



11/13/2006